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Clinical Manifestations, Treatment and Outcomes of Multisystem Inflammatory Syndrome in Children (MIS-C) Associated with COVID-19: A Single-Center Experience from Iran

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ABSTRACT

Background: Multisystem inflammatory syndrome in children (MIS-C) is a documented complication arising from SARS-CoV-2 infection. Even pediatric patients who present with mild initial COVID-19 symptoms may subsequently experience severe morbidity or mortality due to MIS-C; therefore, early identification and prompt clinical management are essential for achieving favorable outcomes. This study aimed to assess the clinical characteristics, therapeutic strategies, and patient outcomes among children diagnosed with MIS-C in Yazd, Iran.

Methods: This study included all pediatric patients admitted to Shahid Sadoughi Hospital in Yazd, Iran, who presented with either suspected or confirmed MIS-C between March 2020 and March 2021. Comprehensive data were extracted from medical records, including demographics, clinical symptoms, laboratory biomarkers, imaging results, and treatment modalities.

Results: The study included 40 children (52.5% males, 47.5% females, median age 7.3 years). Fever was the predominant symptom (87.5%), followed by gastrointestinal complaints (57.5%) and mucocutaneous abnormalities (20%). The digestive, respiratory, and neurological systems were most frequently involved. Hospitalisation lasted 1–7 days in 75% and

8–14 days in 22.5% of patients. Disease severity was severe in 25%, moderate in 47.5%, and mild in 27.5%. Remdesivir (40%), corticosteroids (52.5%), and intravenous immunoglobulin (47.5%) were used as treatment. Notably, the overall mortality rate was 22.5% (9/40), substantially higher than the rates reported in most international studies.

Conclusion: This elevated mortality underscores the urgent need for enhanced early detection, rapid referral systems, and timely immunomodulatory therapy. Previous studies have reported that COVID-19 vaccination is associated with a reduced incidence of MIS-C.

Introduction

SARS-CoV-2, the pathogen responsible for coronavirus disease 2019 (COVID-19), has affected millions of individuals across the world since its emergence in late 2019[1]. Multisystem inflammatory syndrome in children (MIS-C) emerged as a serious post-infectious complication associated with COVID-19[2, 3]. Initial reports of pediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2 (PIMS-TS) originated from Europe and North America in April 2020[4, 5].

The symptoms of MIS-C include persistent fever, multiorgan involvement, and elevated inflammatory markers 2–6 weeks after infection with SARS-CoV-2[6, 7]. While the syndrome exhibits clinical features overlapping with Kawasaki disease, toxic shock syndrome, and macrophage activation syndrome, it has a unique pathophysiology[8, 9]. Consequently, the WHO and CDC adopted case definitions emphasizing fever, multisystem involvement, laboratory evidence of inflammation, and an epidemiological link to COVID-19[10, 11].

The clinical spectrum of MIS-C includes mild illness to life-threatening complications such as myocardial dysfunction, coronary artery abnormalities, shock, and multi-organ failure[12, 13]. Systematic reviews and meta-analyses have indicated mortality rates ranging from 1.7% to 3.9%, with elevated figures observed in middle-income countries[1, 14]. Clinical manifestations include fever (99%), gastrointestinal symptoms (76–88%), mucocutaneous findings (50–65%), and cardiac involvement (55–78%)[15, 16].

Approximately 78% of patients with cardiac complications have abnormal echocardiography, 32–55% have myocardial dysfunction, and 11–22% have coronary artery abnormalities[17, 18]. A majority of MIS-C patients require intensive care unit (ICU) admission, and many require cardiovascular support with inotropes or vasopressors[19, 20]. Inflammatory markers (C-reactive protein, ferritin, D-dimer), lymphopenia, thrombocytopenia, and cardiac biomarkers (troponin, NT-proBNP) are typically elevated in patients[21, 22].

IVIG (intravenous immunoglobulin) together with corticosteroids constitutes the main treatment strategy for MIS-C, whereas biologic agents like anakinra are generally reserved for patients who do not respond to initial treatment[23, 24]. Early administration of combined immunomodulatory therapies has been shown to improve cardiac outcomes in affected children[25, 26]. Respiratory support, fluid resuscitation, and vasopressor support are often necessary[27].

MIS-C data from Middle Eastern countries, especially Iran, remain limited despite growing international literature[28, 29]. Optimizing management protocols requires understanding regional variations in clinical presentation, treatment responses, and outcomes. During the COVID-19 pandemic, this study evaluated the clinical manifestations, treatment approaches, and outcomes of children with MIS-C admitted to a major referral center in Yazd, Iran.

Materials and Methods

Study Design and Setting

This was a single-center, retrospective, observational cohort study conducted at Shahid Sadoughi Hospital, Yazd, Iran — the province's tertiary pediatric referral center and a designated COVID-19 focal point. Using consecutive (census) sampling, all children (<18 years) admitted with suspected or confirmed MIS-C between March 2020 and March 2021 were included. Data were abstracted retrospectively from medical records. (Clinical trial number: not applicable)

Case Definition

MIS-C diagnosis was based on WHO criteria, which include:

- Children and adolescents aged 0–19 years with fever for ≥ 3 days
- Clinical signs of multisystem involvement (at least two of the following): rash or bilateral non-purulent conjunctivitis or mucocutaneous inflammation; hypotension or shock; cardiac dysfunction, pericarditis, valvulitis, or coronary abnormalities; coagulopathy; acute gastrointestinal symptoms
- Elevated markers of inflammation (ESR, CRP, or procalcitonin)
- No other obvious microbial cause of inflammation
- Evidence of COVID-19 (RT-PCR, antigen test, or serology positive) or likely contact with patients with COVID-19

Data Collection

Medical records were retrospectively reviewed to extract comprehensive data including:

- **Demographic information:** Age, sex, anthropometric measurements
- **Clinical manifestations:** Fever, gastrointestinal symptoms (abdominal pain, vomiting, diarrhea), respiratory symptoms, mucocutaneous findings, neurological symptoms
- **Comorbidities:** Pre-existing medical conditions
- Blood tests: Complete blood count, inflammatory markers (C-reactive protein [CRP], erythrocyte sedimentation rate [ESR]), liver and renal function tests, electrolytes, creatine phosphokinase, lactate dehydrogenase, coagulation profile, and, where available, D-dimer. Ferritin, procalcitonin, fibrinogen, troponin and N-terminal pro-B-type natriuretic peptide (NT-proBNP) were not systematically measured across the cohort and are therefore not reported. Microbiological testing: SARS-CoV-2 RT-PCR and serology.
- **Imaging studies:** Chest radiography, chest CT scan, echocardiography
- **Treatment modalities:** Oxygen therapy, antiviral agents (remdesivir), immunomodulatory therapy (IVIG, corticosteroids), biologic agents, supportive care
- **Disease severity:** Classified as mild, moderate, or severe based on clinical presentation, organ involvement, and need for intensive care
- **Outcomes:** Length of hospital stay, ICU admission, complications, mortality

Exclusion Criteria

We excluded children with a significant underlying chronic disease that could confound the presentation, specifically malignancy, pre-existing cardiac disease, or chronic gastrointestinal disease, and records with more than 30% of required variables missing. Of 45 children initially identified, 5 were excluded (2 with hematologic disease, 2 with cardiac disease, and 1 with gastrointestinal disease), leaving 40 patients for analysis.

Disease Severity Classification

Disease severity was categorized as:

- Mild: no supplemental oxygen or respiratory support, no vasoactive/inotropic agents, and no ventricular dysfunction (subclinical or paraclinical involvement only).
- Moderate: requirement for supplemental oxygen by nasal cannula or mask, and/or

limited organ involvement (e.g., coronary changes) without shock.

- Severe: requirement for high-flow oxygen or mechanical ventilation, and/or vasoactive/inotropic support for hypotension or shock, and/or ventricular dysfunction or coronary artery aneurysm (i.e., intensive-care–level support).

Because multi-organ involvement is intrinsic to the MIS-C case definition, it was not used to grade severity; severity was based on objective support requirements and cardiac/hemodynamic status, consistent with the WHO/CDC case definitions and the American Heart Association / American College of Rheumatology guidance.

Statistical Analysis

Statistical analyses were performed using SPSS software version 26.0 (version 26, IBM Corporation, Armonk, NY). Descriptive statistics, such as frequencies, percentages, means, and medians, were calculated. Numbers and percentages were reported for categorical variables, while medians and interquartile ranges were reported for continuous variables. Chi-square test and Fisher's exact test were applied to compare categorical variables, while t-tests or Mann-Whitney U tests were used for continuous variables. Statistical significance was defined as a P value less than 0.05.

Results

Demographic Characteristics

MIS-C was initially identified in 45 children, five of whom had significant underlying chronic conditions and were excluded. Therefore, 40 children were included in the final analysis. **Figure 1** summarizes the demographic characteristics of the study population. Among the participants, 21 were male (52.5%), and 19 were female (47.5%). Half of the patients were aged between 5 and 18 years, with a median age of 7.3 years.

Clinical Manifestations

The clinical manifestations of MIS-C patients are shown in **Figure 2**. Fever was the most frequently observed symptom, occurring in 35 patients (87.5%). The second most common manifestation was gastrointestinal symptoms, occurring in 23 patients (57.5%). Diarrhea, vomiting, and abdominal pain were reported.

Specific frequencies were not provided for all mucocutaneous, respiratory, or neurological symptoms. A descending order of organ system involvement showed that the gastrointestinal, respiratory, and neurological systems were most frequently affected.

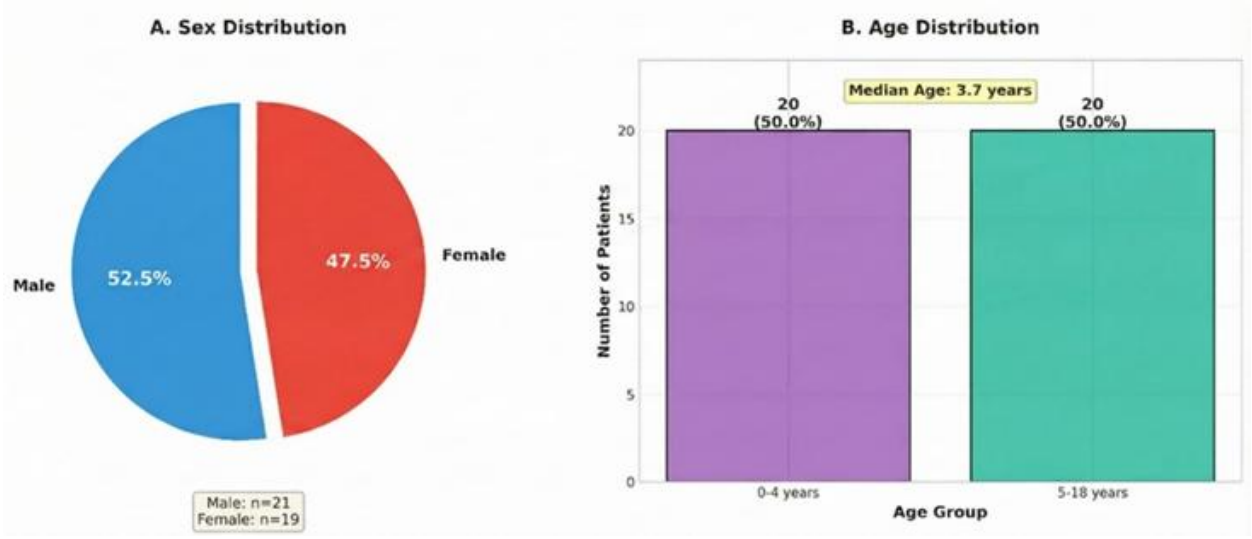

Figure 1. Demographic Characteristics of MIS-C Patients (N = 40)
(A) Sex distribution showing males (n = 21, 52.5%) and females (n = 19, 47.5%). (B) Age distribution across two age groups (0–5 years and 5–18 years); bars indicate patient counts with percentages annotated.

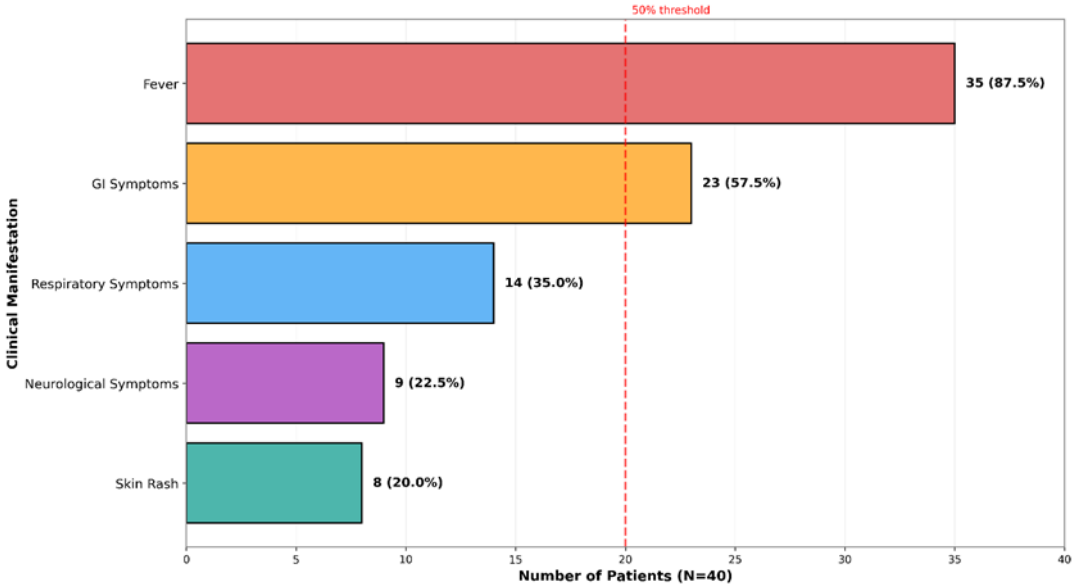

Figure 2. Frequency of Clinical Manifestations in MIS-C Patients.
Horizontal bars represent the number (percentage) of patients with each manifestation: fever (n = 35, 87.5%), gastrointestinal (GI) symptoms (n = 23, 57.5%), respiratory symptoms (n = 14, 35.0%), neurological symptoms (n = 9, 22.5%), and skin rash (n = 8, 20.0%). The dashed vertical line marks the 50% threshold (n = 20). Patients could present with more than one manifestation; therefore, percentages sum to more than 100%. GI: gastrointestinal

Laboratory and Imaging Findings

Laboratory investigations reflected hyperinflammation and multisystem involvement. The most frequent abnormalities were hyponatremia (47.5%), lymphopenia (47.4% of those tested), elevated CRP (37.5%), elevated lactate dehydrogenase (37.5%), elevated ALT (32.5%), hypocalcemia (30%), elevated ESR (30%) and thrombocytopenia (12.5%); SARS-CoV-2 testing was consistent with prior rather than active infection (PCR positive in 27.5%), in keeping with the post-infectious nature of MIS-C (Table 1). Echocardiography was performed in 16 patients (40%) and was abnormal in 11 (68.8% of those studied), including depressed left-ventricular function, coronary artery abnormalities, mitral regurgitation and myocarditis (Table 2). Chest CT was performed in 12 patients (30%) and showed mild, moderate and severe involvement in 1, 5 and 6 patients, respectively (Table 3).

Disease Severity and Hospital Stay

The clinical severity of the disease varied substantially across the cohort (**Figure 3**). Specifically, 10 patients (25%) needed intensive care support, 19 (47.5%) presented with moderate severity characterized by the need for supplemental oxygen and/or limited organ involvement without hemodynamic instability, and 11 (27.5%) exhibited mild disease. Given that MIS-C is a serious condition, the high proportion of moderate to severe cases (72.5% combined) likely reflect

Table 1. Selected laboratory findings at admission (N = 40)

Laboratory parameter	Abnormal, n (%)*
Hyponatremia (Na <135)	19 (47.5)
Lymphopenia	18 of 38 tested (47.4)
Elevated CRP (2+/3+)	15 (37.5)
Elevated LDH (>500)	15 (37.5)
Elevated ALT (>35)	13 (32.5)
Elevated ESR (>30)	12 (30.0)
Hypocalcemia (Ca <8.8)	12 (30.0)
Elevated AST (>45)	10 (25.0)
Elevated BUN	7 of 27 tested (25.9)
Thrombocytopenia (PLT <150k)	5 (12.5)

*Percentages are of the whole cohort unless a denominator of tested patients is shown. CRP: C-reactive protein; LDH: lactate dehydrogenase; ALT: alanine aminotransferase; AST: aspartate aminotransferase; ESR: erythrocyte sedimentation rate; PLT: platelets; BUN: blood urea nitrogen

Table 2. Echocardiographic findings in MIS-C patients (N = 40).

Echocardiographic finding	n (%)
Echocardiography performed	16 (40.0)
Normal study	5 (12.5)
Depressed LV function / low LVEF (any)	7 (17.5)
Coronary artery abnormality (any)	5 (12.5)
Mitral regurgitation (any)	7 (17.5)
Myocarditis (in combination)	4 (10.0)
Not performed/missing	24 (60.0)

Echocardiography was performed in 16 patients (40%); categories are not mutually exclusive. LV: left ventricle; LVEF: left ventricular ejection fraction

Table 3. Chest CT findings in MIS-C patients (N = 40).

Chest CT severity	n (%)
CT performed	12 (30.0)
Mild	1 (2.5)
Moderate	5 (12.5)
Severe	6 (15.0)
Not performed/missing	28 (70.0)

Percentages are of the whole cohort; CT was performed in 12 patients.

the referral pattern to a tertiary care center. Overall, 30 patients (75%) were hospitalized for 1–7 days, 9 (22.5%) for 8–14 days, and 1 (2.5%) for ≥15 days. This distribution must be interpreted with the outcome in mind: because all 9 deaths occurred early in the admission, the short stays are partly outcome-dependent (early mortality)
rather than a reflection of rapid recovery, and length of stay in survivors and non-survivors should not be pooled when interpreting recovery. Patient-level length-of-stay data stratified by survival were not available for separate quantification.

Treatment Modalities

A supportive care approach, antiviral therapy, and immunomodulatory intervention were used (Figure 4). Oxygen therapy was required in 14 patients (35%), representing more than one third of the cohort. Remdesivir was administered to 16 patients (40% of the sample), although its efficacy remains controversial given the post-infectious nature of MIS-C. Treatment was centered on immunomodulatory therapy. Twenty-one patients (52.5%) received corticosteroids, and 19 patients (47.5%) received IVIG.

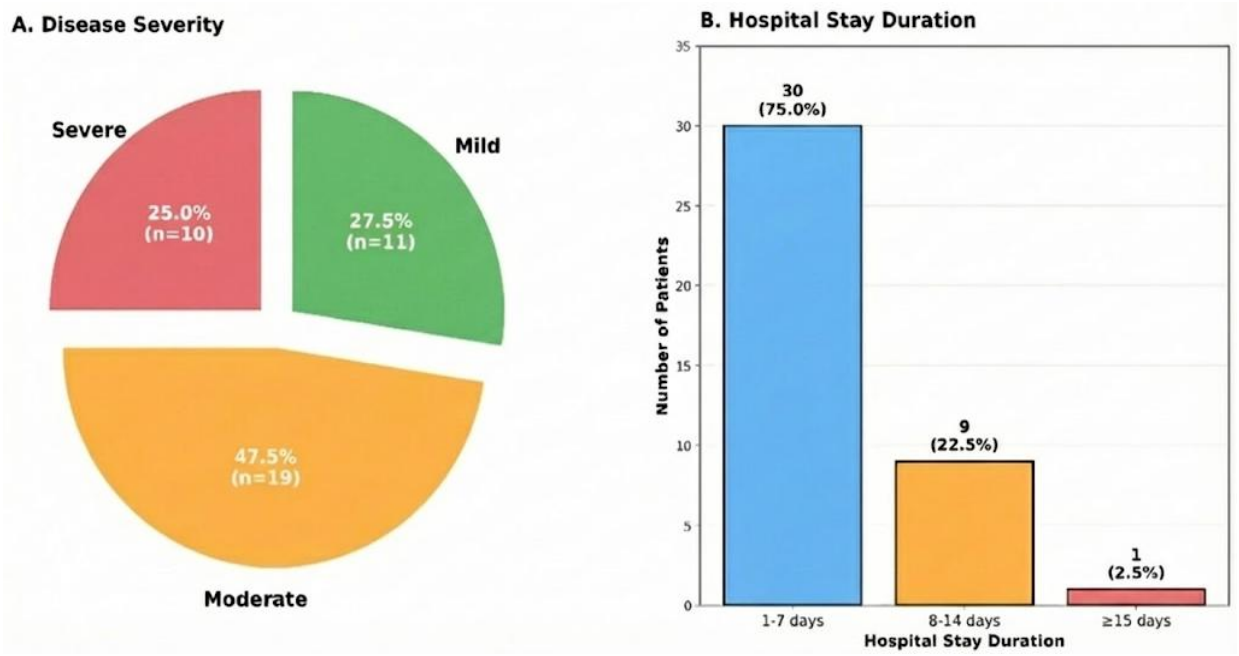

Figure 3. Clinical Severity Profile and Hospitalization Duration in MIS-C (N = 40).
(A) Distribution of clinical severity at presentation: mild (n = 11, 27.5%), moderate (n = 19, 47.5%), and severe (n = 10, 25.0%). (B) Length of hospitalization: 1–7 days (n = 30, 75.0%), 8–14 days (n = 9, 22.5%), and ≥15 days (n = 1, 2.5%). MIS-C: multisystem inflammatory syndrome in children

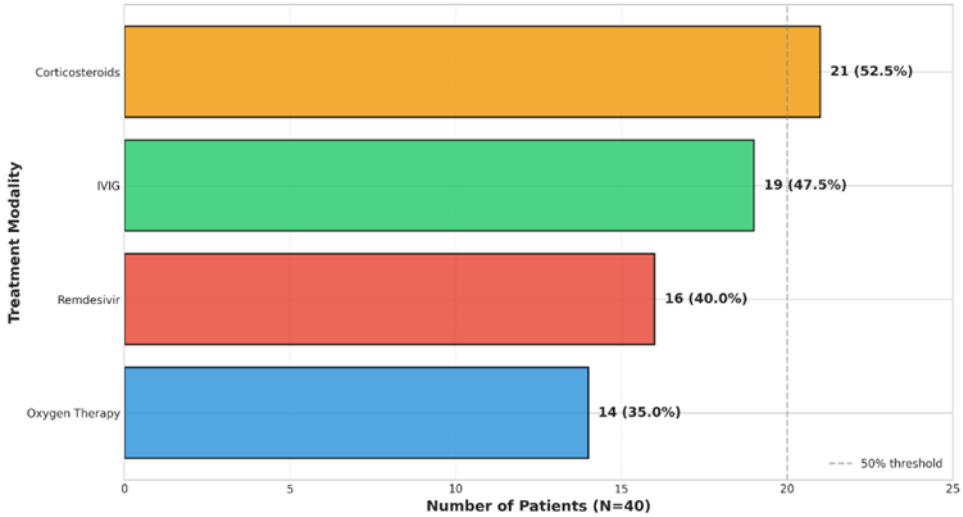

Figure 4. Treatment Modalities Used In MIS-C Management.
Horizontal bars show the number (percentage) of patients who received corticosteroids (n = 21, 52.5%), intravenous immunoglobulin (IVIG) (n = 19, 47.5%), remdesivir (n = 16, 40.0%), and oxygen therapy (n = 14, 35.0%). The dashed vertical line marks the 50% threshold (n = 20). Patients could receive more than one treatment modality; therefore, percentages sum to more than 100%. IVIG: intravenous immunoglobulin

Outcomes

Out of the 40-patient cohort, 22.5% succumbed to the illness, while 31 patients (77.5%) survived to hospital discharge (Figure 5). A strong correlation was observed between clinical outcomes and disease severity classification. Although all 11 patients presenting with mild disease survived, mortality claimed 2 out of 19 patients with moderate disease and 7 out of 10 with severe disease, indicating a high mortality rate among patients requiring intensive care. Hospital stays ranged from 1 to 7 days for 75% of patients, 8–14 days for 22.5%, and 15 days or longer for just 2.5%; however, in some severe cases, this was due to early mortality rather than rapid recovery. Mortality rates are significantly higher in resource-limited settings, likely because of factors such as delayed recognition of the syndrome, limited access to intensive care facilities, and limited availability of immunomodulatory therapies.

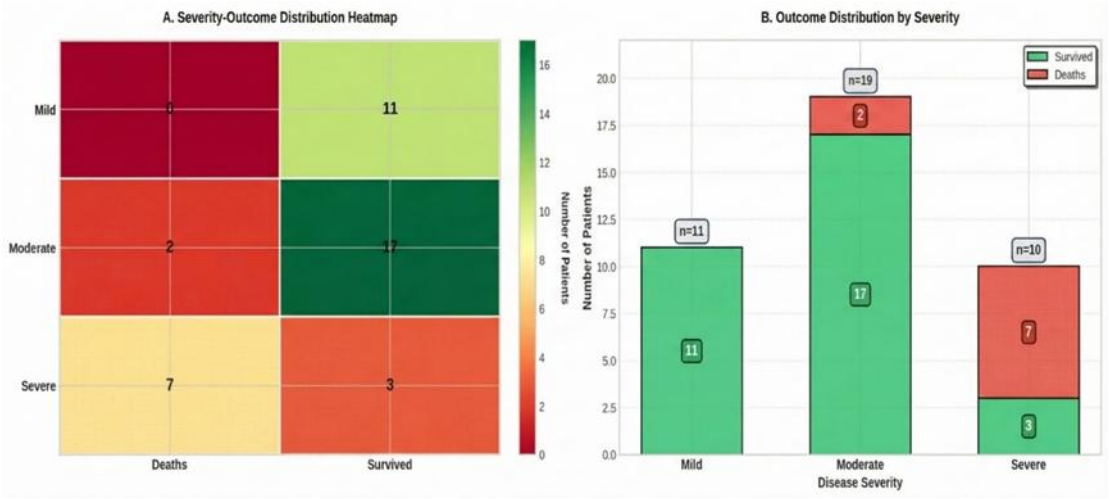

Figure 5. Relationship Between Disease Severity and Clinical Outcomes
(A) Heatmap showing the distribution of clinical outcomes (death vs survival) across severity categories. (B) Stacked bar chart summarizing outcomes by severity: all mild cases survived (11/11), moderate cases included 17 survivors and 2 deaths, and severe cases included 3 survivors and 7 deaths.

Table 4. Mortality stratified by disease severity (N = 40).

Severity	Died, n	Survived, n	Mortality, %
Mild (n = 11)	0	11	0.0
Moderate (n = 19)	2	17	10.5
Severe (n = 10)	7	3	70.0
Severe vs non-severe	OR 32.7 (95% CI 4.5–234)	Fisher P < 0.001	

Severity was defined by objective support requirements (see Methods). The odds ratio compares severe versus non-severe (mild + moderate) disease.

A Fisher's exact test (two-sided) showed a significant association between severity and mortality when severity was categorized as severe versus mild + moderate ($P < 0.001$). Compared with the non-severe group, the odds of death were significantly higher in the severe group (odds ratio 32.7, 95% CI 4.5–234) (Table 4, Table 5).

Table 5. 2×2 Fisher: Severe vs non-Severe

Group	Deaths	Survived
Severe	7	3
Non-severe (Mild + Moderate)	2	28

2×2 Fisher: Severe vs non-severe. Contingency table used for Fisher's exact test comparing mortality between severe MIS-C and non-severe disease (mild + moderate). Values represent counts of deaths and survivors in each group. MIS-C: multisystem inflammatory syndrome in children.

Discussion

MIS-C during the early COVID-19 pandemic waves was characterized by specific clinical characteristics, treatment approaches, and outcomes. In addition to similarities, there are notable differences compared with international reports.

Clinical Presentation

In our cohort, MIS-C showed a clinical profile comparable to that reported in the international literature. Fever was present in 87.5% of patients, which is slightly below the nearly universal frequency of approximately 99% reported in pooled analyses[30, 31]. This may reflect variations in case definition application or documentation. We found gastrointestinal symptoms in 57.5% of our patients, slightly lower than the 76–88% reported in systematic reviews[15, 16]. The pathophysiology of MIS-C includes widespread endothelial dysfunction and hyperinflammation, both of which are associated with GI and cardiac involvement[32, 33].

The median age of 7.3 years in our cohort was also consistent with international data indicating that MIS-C predominantly affects school-age children and adolescents[34, 35]. MIS-C differs from classic Kawasaki disease, which usually affects children younger than 5 years[36, 37]. Our study found an equal distribution of patients across age groups (50% aged 0–5 years and 50% aged 5–18 years).

Disease Severity and Complications

In our cohort, 25% of patients were classified as severe, 47.5% as moderate, and 27.5% as mild, meaning that 72.5% presented with moderate to severe disease. According to reports, approximately 50–53% of MIS-C patients require ICU admission[38, 39]. A high proportion of moderate-to-severe cases in our study may reflect both the severity of MIS-C and the concentration of critically ill patients in tertiary centers. MIS-C is characterized by cardiac involvement, though specific frequencies of myocardial dysfunction and coronary abnormalities were not detailed in our cohort. Previous studies have shown that 55–78% of patients have abnormal echocardiographic findings, 32–55% experience myocardial dysfunction, and 11–22% develop coronary artery abnormalities[40–42]. In contrast to acute COVID-19, respiratory manifestations in MIS-C are generally less prominent[43, 44]. Depending on the cohort and definition, neurological involvement varies from 4% to 28%[45, 46].

Treatment Approaches

In our study, we noted both adherence to and deviation from international guidelines. While IVIG and corticosteroids are recognized as the main treatments for MIS-C[47, 48], our cohort received 52.5% corticosteroids and 47.5% IVIG,

compared with 78–88% IVIG and 63–75% corticosteroids in larger pooled data[49, 50].

Our cohort had lower rates of immunomodulatory therapy for several reasons. First, treatment protocols were still evolving during the early pandemic (2020–2021), and evidence for optimal therapy was limited. Second, middle-income countries may not have access to IVIG due to resource constraints[51, 52]. The third reason is that some patients died before immunomodulatory therapy could be administered. In addition, treatment thresholds and severity assessments varied.

During the early phase of the pandemic, remdesivir was administered to 40% of patients. The antiviral activity of remdesivir against SARS-CoV-2 is questionable, as MIS-C is a post-infectious inflammatory syndrome rather than an acute viral infection[53, 54]. For this reason, routine use of antiviral therapy in MIS-C is generally not recommended except in cases of concurrent COVID-19 infection[8, 47, 55, 56]. Furthermore, 35% of patients required oxygen therapy, indicating respiratory compromise. The respiratory system is involved in 28–39% of MIS-C cases[57, 58]. In such patients, the need for oxygen therapy may be explained by both pulmonary involvement and associated cardiac dysfunction.

Mortality and Outcomes

We found a mortality rate of 22.5%, substantially higher than the 1.7–3.9% reported in systematic reviews and meta-analyses[59–61]. Clinical practice and public health policy in Iran should consider this elevated mortality. Our cohort's higher mortality may be explained by several factors. This comparison should be interpreted with caution, because differences in case definitions (WHO versus CDC), referral and selection bias inherent to a single tertiary center that concentrates the most severe cases, and the high proportion of moderate-to-severe disease in our cohort may all inflate the apparent mortality relative to population-based international series.

1. **Delayed Presentation:** MIS-C was not widely known during the early pandemic. In the event of delayed recognition, patients may have presented with advanced disease and established organ failure[62, 63]. A timely diagnosis and immunomodulatory therapy improve outcomes[64, 65].
2. **Resource Limitations:** Healthcare infrastructure in middle-income countries is limited by limited ICU capacity, advanced monitoring equipment, and expensive medications (especially IVIG)[2, 66]. Middle-income countries have higher mortality rates than high-income settings, according to Yasuhara et al.[1].
3. **Treatment Delays and Suboptimal Therapy:** Immunomodulatory therapy use in our cohort (52.5% corticosteroids, 47.5% IVIG) was lower than international standards (78–88% IVIG, 63–75% corticosteroids) and may have contributed to worse outcomes, although this observational study cannot establish a causal relationship[67, 68]. Early combined immunomodulatory therapy has been reported to reduce cardiac complications and improve recovery[69, 70].
4. **Comorbidities and Risk Factors:** We excluded patients with significant underlying chronic diseases, but milder comorbidities may have been present. In some cohorts, obesity was associated with more severe MIS-C[71, 72]. Mortality has been associated with comorbidities in several case studies[44, 73].
5. **Severity of Presentation:** Referrals to tertiary centers may represent the most severe cases. We found a high proportion of moderate-to-severe disease (72.5%) in our cohort[74, 75].
6. **Laboratory and Clinical Predictors:** Iron levels, D-dimer levels, NT-proBNP levels, and troponin levels are associated with severity and poor outcomes[8, 76]. Heart disease, acute kidney injury, and need for vasopressors are strongly associated with mortality[77, 78]. For risk stratification, detailed analysis of these biomarkers would be useful.

Comparison with Iranian Studies

MIS-C outcomes from Iran are scarce, making our findings particularly useful. The clinical characteristics of the Rostami-Maskopaee et al. cohort are similar to ours[28]. Other Iranian studies have focused on gastrointestinal manifestations and radiographic features[79, 80]. However, patient populations, treatment protocols, and study periods may differ from those reported by some Iranians[81].

Implications for Clinical Practice

In Iran and similar settings, our findings have several important implications:

1. **Enhanced Awareness and Education:** Pediatricians, emergency department staff, and primary care physicians need to be aware of MIS-C. In educational programs, clinical features and diagnostic criteria should be emphasized[82, 83].
2. **Early Diagnosis and Referral:** A clear referral pathway and criteria can reduce delays in diagnosis and treatment. Inflammatory and cardiac biomarkers can be assessed at the point of care[84, 85].
3. **Standardized Treatment Protocols:** A combination of IVIG and corticosteroids, as early combined immunomodulatory therapy, may improve outcomes. Protocols should be adapted to resource-constrained settings[86, 87].
4. **Multidisciplinary Care:** For MIS-C management, healthcare systems should provide IVIG, corticosteroids, and intensive care[83, 88]. Strategic stockpiling is recommended during pandemic surges[39, 89].
5. **Follow-up and Long-term Monitoring:** Follow-up after MIS-C is necessary to monitor persistent cardiac abnormalities, inflammation, and psychosocial effects. PICU survivors report persistent physical symptoms at 1-year follow-up in 62% of studies[19, 50].

Prevention and Vaccination

By preventing SARS-CoV-2 infection, the burden of MIS-C can be reduced. COVID-19 vaccines are effective in preventing acute infection and post-infectious complications, including MIS-C[90, 91]. The incidence of MIS-C is low among vaccinated adolescents[92, 93]. Children and adolescents need higher vaccination coverage to prevent both acute COVID-19 and MIS-C in Iran.

Study Limitations

There are some limitations. First, the single-center retrospective design limits generalizability and introduces selection bias. Second, the relatively small sample size (n = 40) reduces statistical power for subgroup analyses. Third, detailed laboratory results, echocardiographic findings, and specific treatment regimens were not fully captured in the available data, limiting predictor analysis. Fourth, the study period (2020-2021) represents early pandemic management when knowledge and resources were limited; outcomes could have improved. Fifth, long-term follow-up data are not available to assess persistent sequelae.

Future Directions

We recommend larger, multicenter prospective studies of MIS-C across Iran to characterize regional variations, identify mortality risk factors, and evaluate treatment protocols. Future research should focus on:

1. **Risk Stratification:** Predicting severity of disease and evaluating treatment efficacy using clinical and laboratory scores
2. **Treatment Optimization:** Comparing immunomodulatory regimens, timing, and biologic agents for Iranians
3. **Long-term Outcomes:** Evaluation of various treatment strategies and vaccination programs in Iran
4. **Health Economics:** Cost-effectiveness analyses of different treatment strategies and vaccination programs in the Iranian context
5. **Genetic and Immunologic Studies:** Determining genetic factors and immune profiles that may be associated with MIS-C

Conclusion

This study describes the clinical characteristics, treatment patterns, and

outcomes of MIS-C among children treated at a tertiary pediatric center in Yazd, Iran. Clinical features included fever, gastrointestinal symptoms, and multisystem involvement, consistent with international reports. However, the mortality rate of 22.5% was markedly higher than that reported in most international studies, likely reflecting delayed presentation, resource limitations, and inadequate treatment.

Our findings support existing recommendations that emphasize early recognition of MIS-C, prompt referral, and timely immunomodulatory therapy in children who present with fever and multisystem symptoms during or after COVID-19 surges. As an observational study, our data cannot demonstrate the efficacy of any specific treatment; the elevated mortality should therefore be regarded as hypothesis-generating. Previous studies indicate that COVID-19 vaccination is associated with a reduced incidence of MIS-C, and ensuring the availability of IVIG, intensive-care capacity, and specialized expertise may support MIS-C management in comparable settings.

There is also a need to strengthen MIS-C epidemiological data across Iran, identify predictors of mortality, refine treatment strategies, and improve patient outcomes through large multicenter studies. International collaboration and knowledge sharing can reduce mortality in resource-limited settings. A proactive approach, early diagnosis, evidence-based treatment, and comprehensive vaccination programs can dramatically reduce MIS-C mortality. Clinicians and policymakers can learn from this study to better protect children from COVID-19 complications.

Abbreviations

COVID-19: Coronavirus disease 2019; MIS-C: Multisystem inflammatory syndrome in children; SARS-CoV-2: Severe acute respiratory syndrome coronavirus 2; PIMS-TS: Pediatric inflammatory multisystem syndrome temporally associated with SARS-CoV-2; WHO: World Health Organization; CDC: Centers for Disease Control and Prevention; ICU: Intensive care unit; IVIG: Intravenous immunoglobulin; RT-PCR: Reverse transcription polymerase chain reaction; CRP: C-reactive protein; ESR: Erythrocyte sedimentation rate; NT-proBNP: N-terminal pro-B-type natriuretic peptide; LVEF: Left ventricular ejection fraction; ECMO: Extracorporeal membrane oxygenation.

Conflict of Interest

Not applicable.

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Ethical Considerations

This study was approved by the Ethics Committee of Shahid Sadoughi University of Medical Sciences, Yazd, Iran. (Ethics Code: IR.SSU.MEDICINE.REC.1403.102) Due to the retrospective nature of the study, the requirement for informed consent was waived by the ethics committee. All procedures performed in this study were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki Declaration and its later amendments. (Clinical trial number: not applicable).

AI Disclosure

Artificial intelligence–based tools were used solely to assist with language editing and

formatting. The authors reviewed and verified all content and take full responsibility for the integrity and accuracy of the manuscript. Specifically, Claude Sonnet 5 (Anthropic), operated via Claude Code, was used for language editing and formatting only.

Author's Contribution

Conceptualizing the study, collecting data, and contributing to drafting the manuscript: N.V. B.; Supervising the study, providing clinical expertise, and revising the manuscript: F. F.; Providing clinical guidance and reviewing patient management: M. K., N. N., and Z. N. Performing the statistical analysis and writing the first draft: M. E. SH.; Reviewing and completing the final edit: S. S. All authors read and approved the final manuscript.

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References

1. Yasuhara J, Watanabe K, Takagi H, Sumitomo N, Kuno T. COVID-19 and multisystem inflammatory syndrome in children: A systematic review and meta-analysis. Pediatr Pulmonol. 2021;56(5):837-48.
2. Patel JM. Multisystem Inflammatory Syndrome in Children (MIS-C). Curr Allergy Asthma Rep. 2022;22(5):53-60.
3. Feldstein LR, Rose EB, Horwitz SM, Collins JP, Newhams MM, Son MBF, et al. Multisystem Inflammatory Syndrome in U.S. Children and Adolescents. N Engl J Med. 2020;383(4):334-46.
4. Riphagen S, Gomez X, Gonzalez-Martinez C, Wilkinson N, Theocharis P. Hyperinflammatory shock in children during COVID-19 pandemic. Lancet. 2020;395(10237):1607-8.
5. Verdoni L, Mazza A, Gervasoni A, Martelli L, Ruggeri M, Ciuffreda M, et al. An outbreak of severe Kawasaki-like disease at the Italian epicentre of the SARS-CoV-2 epidemic: an observational cohort study. Lancet. 2020;395(10239):1771-8.
6. Consiglio CR, Cotugno N, Sardh F, Pou C, Amodio D, Rodriguez L, et al. The Immunology of Multisystem Inflammatory Syndrome in Children with COVID-19. Cell. 2020;183(4):968-81.e7.
7. Modarresi SZ, Savabieh S, Naserzadeh N, Yazdanparast M, Talaeipour S. Multisystem Inflammatory Syndrome in Children (MIS-C): A Review of Short- and Long-Term Complications. Iran J Ped Hematol Oncol. 2026;16(1):788-805
8. Henderson LA, Canna SW, Friedman KG, Gorelik M, Lapidus SK, Bassiri H, et al. American College of Rheumatology Clinical Guidance for Multisystem Inflammatory Syndrome in Children Associated With SARS-CoV-2 and Hyperinflammation in Pediatric COVID-19: Version 3. Arthritis Rheumatol. 2022;74(4):e1-e20.
9. Kaushik A, Gupta S, Sood M, Sharma S, Verma S. A Systematic Review of Multisystem Inflammatory Syndrome in Children Associated With SARS-CoV-2 Infection. Pediatr Infect Dis J. 2020;39(11):e340-e6.
10. World Health O. Multisystem inflammatory syndrome in children and adolescents temporally related to COVID-19. Geneva: World Health Organization; 2020.
11. Centers for Disease C, Prevention. Multisystem inflammatory syndrome in children (MIS-C) associated with coronavirus disease 2019 (COVID-19). Atlanta: Centers for Disease Control and Prevention; 2020.
12. Belhadjer Z, Méot M, Bajolle F, Khraiche D, Legendre A, Abakka S, et al. Acute Heart Failure in Multisystem Inflammatory Syndrome in Children in the Context of Global SARS-CoV-2 Pandemic. Circulation 2020; 142(5): 429-36.
13. Whittaker E, Bamford A, Kenny J, Kaforou M, Jones CE, Shah P, et al. Clinical Characteristics of 58 Children With a Pediatric Inflammatory Multisystem Syndrome Temporally Associated With SARS-CoV-2. JAMA 2020; 324(3): 259-69.
14. Shyong O, Alfakhri N, Bates SV, Carroll RW, Gallagher K, Huang L, et al. Multisystem Inflammatory Syndrome in Children: A Comprehensive Review Over the Past Five

Years. J Intensive Care Med. 2025: 8850666251320558.
15. Tang Y, Li W, Baskota M, Zhou Q, Fu Z, Luo Z, et al. Multisystem inflammatory syndrome in children during the coronavirus disease 2019 (COVID-19) pandemic: a systematic review of published case studies. Transl Pediatr 2021; 10(1): 121-35.
16. Guimarães D, Pissarra R, Reis-Melo A, Guimarães H. Multisystem inflammatory syndrome in children (MISC): A systematic review. Int J Clin Pract 2021; 75(11): e14450.
17. Kamfar S, Zeinali V, Alaei F, Farahbakhsh N, Tabatabaee S, Mosallanejad A. COVID-19 Related Multi-System Inflammatory Syndrome in Children (MIS-C): A Systematic Review. Archives of Pediatric Infectious Diseases 2024; 12(3): e139928.
18. Rabinowicz S, Leshem E, Pessach IM. COVID-19 in the Pediatric Population-Review and Current Evidence. Curr Infect Dis Rep 2020; 22(11): 29.
19. Seijbel TC, Hoste L, Buysse CMP, Dulfer K, Haerynck F, de Hoog M, Ketharanathan N. Multidimensional 1-Year Outcomes After Intensive Care Admission for Multisystem Inflammatory Syndrome in Children. Crit Care Explor 2025; 7(1): e1213.
20. Shekerdemian LS, Mahmood NR, Wolfe KK, Riggs BJ, Ross CE, McKiernan CA, et al. Characteristics and Outcomes of Children With Coronavirus Disease 2019 (COVID-19) Infection Admitted to US and Canadian Pediatric Intensive Care Units. JAMA Pediatr. 2020;174(9):868-73.
21. Albanji MH, Baghafar AA, Alghanmi YA, Shaaban MM, Alkashlan EA, Sende HH, et al. Clinical Presentation and Management of Multisystem Inflammatory Syndrome in Children With COVID-19: A Systematic Review. Cureus 2023; 15(10): e46918.
22. Lampidi S, Maritsi D, Charakida M, Eleftheriou I, Farmaki E, Spyridis N, et al. Multisystem inflammatory syndrome in children (MIS-C): A nationwide collaborative study in the Greek population. Eur J Pediatr 2024; 183(4): 1693-702.
23. Henderson LA. COVID-19-Related Multisystemic Inflammatory Syndrome in Children (MIS-C). Adv Exp Med Biol 2024; 1448: 409-25.
24. Son MBF, Murray N, Friedman K, Young CC, Newhams MM, Feldstein LR, et al. Multisystem Inflammatory Syndrome in Children - Initial Therapy and Outcomes. N Engl J Med 2021; 385(1): 23-34.
25. McArdle AJ, Vito O, Patel H, Seaby EG, Shah P, Wilson C, et al. Treatment of Multisystem Inflammatory Syndrome in Children. N Engl J Med 2021; 385(1): 11-22.
26. Ouldali N, Toubiana J, Antona D, Javouhey E, Madhi F, Lorrot M, et al. Association of Intravenous Immunoglobulins Plus Methylprednisolone vs Immunoglobulins Alone With Course of Fever in Multisystem Inflammatory Syndrome in Children. JAMA 2021; 325(9): 855-64.
27. Al Rawahi H, Al Ismaili R, Al Zeidi A, Al Farsi A, Al Waili B, Al Noobi B, et al. Multisystem Inflammatory Syndrome in Children: A Multicenter Retrospective Study. Dr Sulaiman Al Habib Medical Journal 2024; 6(2): 58-65.
28. Rostami-Maskopaee F, Ladomenou F, Razavi-Amoli SK, Navaeifar MR, Hajialibeig A, Shahbaznejad L, et al. Clinical characteristics and outcomes of the multisystem inflammatory syndrome in children (MIS-C) following COVID-19 infection in Iran: A multicenter study. PLoS One 2022; 17(9): e0274104.
29. Armin S, Fahimzad SA, Rafiei Tabatabaei S, Mansour Ghanaiee R, Marhamati N, Ahmadizadeh SN, et al. COVID-19 Mortality in Children: A Referral Center Experience from Iran (Mofid Children's Hospital, Tehran, Iran). Can J Infect Dis Med Microbiol 2022; 2022: 2737719.
30. Abrams JY, Oster ME, Godfred-Cato SE, Bryant B, Datta SD, Campbell AP, et al. Factors linked to severe outcomes in multisystem inflammatory syndrome in children (MIS-C) in the USA: a retrospective surveillance study. Lancet Child Adolesc Health 2021; 5(5): 323-31.
31. Jonat B, Gorelik M, Boneparth A, Geneslaw AS, Zachariah P, Shah A, et al. Multisystem Inflammatory Syndrome in Children Associated With Coronavirus Disease 2019 in a Children's Hospital in New York City: Patient Characteristics and an Institutional Protocol for Evaluation, Management, and Follow-Up. Pediatr Crit Care Med 2021; 22(3): e178-e91.

32. Viner RM, Whittaker E. Kawasaki-like disease: emerging complication during the COVID-19 pandemic. Lancet 2020; 395(10239): 1741-3.
33. Rowley AH. Understanding SARS-CoV-2-related multisystem inflammatory syndrome in children. Nat Rev Immunol 2020; 20(8): 453-4.
34. Godfred-Cato S, Bryant B, Leung J, Oster ME, Conklin L, Abrams J, et al. COVID-19-Associated Multisystem Inflammatory Syndrome in Children - United States, March-July 2020. MMWR Morb Mortal Wkly Rep 2020; 69(32): 1074-80.
35. Morris SB, Schwartz NG, Patel P, Abbo L, Beauchamps L, Balan S, et al. Case Series of Multisystem Inflammatory Syndrome in Adults Associated with SARS-CoV-2 Infection - United Kingdom and United States, March-August 2020. MMWR Morb Mortal Wkly Rep 2020; 69(40): 1450-6.
36. McCrindle BW, Rowley AH, Newburger JW, Burns JC, Bolger AF, Gewitz M, et al. Diagnosis, Treatment, and Long-Term Management of Kawasaki Disease: A Scientific Statement for Health Professionals From the American Heart Association. Circulation. 2017;135(17):e927-e99.
37. Ae R, Makino N, Kosami K, Kuwabara M, Matsubara Y, Nakamura Y. Epidemiology, Treatments, and Cardiac Complications in Patients with Kawasaki Disease: The Nationwide Survey in Japan, 2017-2018. J Pediatr 2020; 225: 23-9.e2.
38. Miller J, Cantor A, Zachariah P, Ahn D, Martinez M, Margolis KG. Gastrointestinal Symptoms as a Major Presentation Component of a Novel Multisystem Inflammatory Syndrome in Children That Is Related to Coronavirus Disease 2019: A Single Center Experience of 44 Cases. Gastroenterology. 2020;159(4):1571-4.e2.
39. Ramcharan T, Nolan O, Lai CY, Prabhu N, Krishnamurthy R, Richter AG, et al. Paediatric Inflammatory Multisystem Syndrome: Temporally Associated with SARS-CoV-2 (PIMS-TS): Cardiac Features, Management and Short-Term Outcomes at a UK Tertiary Paediatric Hospital. Pediatr Cardiol. 2020;41(7):1391-401.
40. Matsubara D, Kauffman HL, Wang Y, Calderon-Anyosa R, Nadaraj S, Elias MD, et al. Echocardiographic Findings in Pediatric Multisystem Inflammatory Syndrome Associated With COVID-19 in the United States. J Am Coll Cardiol 2020; 76(17): 1947-61.
41. Feldstein LR, Tenforde MW, Friedman KG, Newhams M, Rose EB, Dapul H, et al. Characteristics and Outcomes of US Children and Adolescents With Multisystem Inflammatory Syndrome in Children (MIS-C) Compared With Severe Acute COVID-19. JAMA 2021; 325(11): 1074-87.
42. Valverde I, Singh Y, Sanchez-de-Toledo J, Theocharis P, Chikermane A, Di Filippo S, et al. Acute Cardiovascular Manifestations in 286 Children With Multisystem Inflammatory Syndrome Associated With COVID-19 Infection in Europe. Circulation 2021; 143(1): 21-32.
43. Castagnoli R, Votto M, Licari A, Brambilla I, Bruno R, Perlini S, et al. Severe Acute Respiratory Syndrome Coronavirus 2 (SARS-CoV-2) Infection in Children and Adolescents: A Systematic Review. JAMA Pediatr 2020; 174(9): 882-9.
44. Götzinger F, Santiago-García B, Noguera-Julián A, Lanaspa M, Lancella L, Calò Carducci FI, et al. COVID-19 in children and adolescents in Europe: a multinational, multicentre cohort study. Lancet Child Adolesc Health 2020; 4(9): 653-61.
45. Schupper AJ, Yaeger KA, Morgenstern PF. Neurological manifestations of pediatric multi-system inflammatory syndrome potentially associated with COVID-19. Childs Nerv Syst 2020; 36(8): 1579-80.
46. LaRovere KL, Riggs BJ, Poussaint TY, Young CC, Newhams MM, Maamari M, et al. Neurologic Involvement in Children and Adolescents Hospitalized in the United States for COVID-19 or Multisystem Inflammatory Syndrome. JAMA Neurol 2021; 78(5): 536-47.
47. American Academy of P. Multisystem inflammatory syndrome in children (MIS-C) interim guidance. Itasca: American Academy of Pediatrics; 2021.
48. Royal College of P, Child H. Paediatric multisystem inflammatory syndrome temporally associated with COVID-19 (PIMS) - guidance for clinicians. London: Royal College of Paediatrics and Child Health; 2021.
49. Ouldali N, Bagheri H, Salvo F, Antona D, Pariente A, Leblanc C, et al. Hyper inflammatory syndrome following COVID-19

mRNA vaccine in children: A national post-authorization pharmacovigilance study. Lancet Reg Health Eur 2022; 17: 100393.
50. Penner J, Abdel-Mannan O, Grant K, Maillard S, Kucera F, Hassell J, et al. 6-month multidisciplinary follow-up and outcomes of patients with paediatric inflammatory multisystem syndrome (PIMS-TS) at a UK tertiary paediatric hospital: a retrospective cohort study. Lancet Child Adolesc Health. 2021; 5(7): 473-82.
51. Belot A, Antona D, Renolleau S, Javouhey E, Hentgen V, Angoulvant F, et al. SARS-CoV-2-related paediatric inflammatory multisystem syndrome, an epidemiological study, France, 1 March to 17 May 2020. Euro Surveill. 2020; 25(22).
52. Pouletty M, Borocco C, Ouldali N, Caseris M, Basmaci R, Lachaume N, et al. Paediatric multisystem inflammatory syndrome temporally associated with SARS-CoV-2 mimicking Kawasaki disease (Kawa-COVID-19): a multicentre cohort. Ann Rheum Dis. 2020; 79(8): 999-1006.
53. Goldman JD, Lye DCB, Hui DS, Marks KM, Bruno R, Montejano R, et al. Remdesivir for 5 or 10 Days in Patients with Severe Covid-19. N Engl J Med 2020; 383(19): 1827-37.
54. Spinner CD, Gottlieb RL, Criner GJ, Arribas López JR, Cattelan AM, Soriano Viladomiu A, et al. Effect of Remdesivir vs Standard Care on Clinical Status at 11 Days in Patients With Moderate COVID-19: A Randomized Clinical Trial. JAMA 2020; 324(11): 1048-57.
55. Bhumbra S, Malin S, Kirkpatrick L, Khaitan A, John CC, Rowan CM, Enane LA. Clinical Features of Critical Coronavirus Disease 2019 in Children. Pediatr Crit Care Med. 2020; 21(10): e948-e53.
56. DeBiasi RL, Song X, Delaney M, Bell M, Smith K, Pershad J, et al. Severe Coronavirus Disease-2019 in Children and Young Adults in the Washington, DC, Metropolitan Region. J Pediatr 2020; 223: 199-203.e1.
57. Brumfiel CM, DiLorenzo AM, Petronic-Rosic VM. Dermatologic manifestations of COVID-19-associated multisystem inflammatory syndrome in children. Clin Dermatol 2021; 39(2): 329-33.
58. Swann OV, Holden KA, Turtle L, Pollock L, Fairfield CJ, Drake TM, et al. Clinical characteristics of children and young people admitted to hospital with covid-19 in United Kingdom: prospective multicentre observational cohort study. BMJ 2020; 370: m3249.
59. Kapoor R, Chandra T, Singh CP, Singh R, Pandey I. Multisystem Inflammatory Syndrome in Children (MIS-C) Related to SARS-CoV-2 and 1-Year Follow-up. Indian J Pediatr 2023; 90(10): 1008-12.
60. Pawar R, Gavade V, Patil N, Mali V, Girwalkar A, Tarkasband V, et al. Neonatal Multisystem Inflammatory Syndrome (MIS-N) Associated with Prenatal Maternal SARS-CoV-2: A Case Series. Children (Basel). 2021; 8(7): 572.
61. Bustos BR, Jaramillo-Bustamante JC, Vasquez-Hoyos P, Cruces P, Díaz F. Pediatric Inflammatory Multisystem Syndrome Associated With SARS-CoV-2: A Case Series Quantitative Systematic Review. Pediatr Emerg Care 2021; 37(1): 44-7.
62. Radia T, Williams N, Agrawal P, Harman K, Weale J, Cook J, Gupta A. Multi-system inflammatory syndrome in children & adolescents (MIS-C): A systematic review of clinical features and presentation. Paediatr Respir Rev 2021; 38: 51-7.
63. Elias MD, McCrindle BW, Larios G, Choueiter NF, Dahdah N, Harahsheh AS, et al. Management of Multisystem Inflammatory Syndrome in Children Associated With COVID-19: A Survey From the International Kawasaki Disease Registry. CJC Open 2020; 2(6): 632-40.
64. Harthan AA, Nadiger M, McGarvey JS, Hanson K, Gharpure VP, Bjornstad EC, et al. Early combination therapy with immunoglobulin and steroids is associated with shorter ICU length of stay in Multisystem Inflammatory Syndrome in Children (MIS-C) associated with COVID-19: A retrospective cohort analysis from 28 U.S. Hospitals. Pharmacotherapy 2022; 42(7): 529-39.
65. Schlapbach LJ, Andre MC, Grazioli S, Schöbi N, Ritz N, Aebi C, et al. Best Practice Recommendations for the Diagnosis and Management of Children With Pediatric Inflammatory Multisystem Syndrome Temporally Associated With SARS-CoV-2 (PIMS-TS; Multisystem Inflammatory Syndrome in Children, MIS-C) in Switzerland. Frontiers in Pediatrics. 2021;Volume 9 - 2021.

66. Buonsenso D, Munblit D, De Rose C, Sinatti D, Ricchiuto A, Carfi A, Valentini P. Preliminary evidence on long COVID in children. Acta Paediatr 2021; 110(7): 2208-11.
67. Batu ED, Demirkan FG, Sag E, Lamot L, Faleye A, Marrani E, et al. The impact of the COVID-19 pandemic on pediatric rheumatology practice: an international, cross-sectional survey study. Semin Arthritis Rheum 2023; 63: 152289.
68. Licciardi F, Pruccoli G, Denina M, Parodi E, Taglietto M, Rosati S, Montin D. SARS-CoV-2-Induced Kawasaki-Like Hyperinflammatory Syndrome: A Novel COVID Phenotype in Children. Pediatrics 2020; 146(2): e20201711.
69. Koné-Paut I, Cimaz R. Is it Kawasaki shock syndrome, Kawasaki-like disease or pediatric inflammatory multisystem disease? The importance of semantic in the era of COVID-19 pandemic. RMD Open 2020; 6(2): e001333.
70. Grimaud M, Starck J, Levy M, Marais C, Chareyre J, Khraiche D, et al. Acute myocarditis and multisystem inflammatory emerging disease following SARS-CoV-2 infection in critically ill children. Ann Intensive Care 2020; 10(1): 69.
71. Kompaniyets L, Agathis NT, Nelson JM, Preston LE, Ko JY, Belay B, et al. Underlying Medical Conditions Associated With Severe COVID-19 Illness Among Children. JAMA Netw Open 2021; 4(6): e2111182.
72. Zachariah P, Johnson CL, Halabi KC, Ahn D, Sen AI, Fischer A, et al. Epidemiology, Clinical Features, and Disease Severity in Patients With Coronavirus Disease 2019 (COVID-19) in a Children's Hospital in New York City, New York. JAMA Pediatr. 2020;174(10):e202430.
73. Preston LE, Chevinsky JR, Kompaniyets L, Lavery AM, Kimball A, Boehmer TK, Goodman AB. Characteristics and Disease Severity of US Children and Adolescents Diagnosed With COVID-19. JAMA Netw Open 2021; 4(4): e215298.
74. Moreira A, Chorath K, Rajasekaran K, Burmeister F, Ahmed M, Moreira A. Demographic predictors of hospitalization and mortality in US children with COVID-19. Eur J Pediatr. 2021; 180(5): 1659-63.
75. Graff K, Smith C, Silveira L, Jung S, Curran-Hays S, Jarjour J, et al. Risk Factors for Severe COVID-19 in Children. Pediatr Infect Dis J 2021; 40(4): e137-e45.
76. Hameed S, Elbaaly H, Reid CEL, Santos RMF, Shivamurthy V, Wong J, Jogeesvaran KH. Spectrum of Imaging Findings at Chest Radiography, US, CT, and MRI in Multisystem Inflammatory Syndrome in Children Associated with COVID-19. Radiology 2021; 298(1): E1-e10.
77. Jain S, Sen S, Lakshmivenkateshiah S, Bobhate P, Venkatesh S, Udani S, et al. Multisystem Inflammatory Syndrome in Children With COVID-19 in Mumbai, India. Indian Pediatr 2020; 57(11): 1015-9.
78. Shah SS, Naidu PKK, Selvam S, Shetty R, Bhat CS, Maheshwari S. Cardiac findings in multisystem inflammatory syndrome in children: Short term follow up in a large Indian series. Ann Pediatr Cardiol. 2023;16(2):94-101.
79. Shahbaznejad L, Navaeifar MR, Abbaskhanian A, Hosseinzadeh F, Rahimzadeh G, Rezai MS. Clinical characteristics of 10 children with a pediatric inflammatory multisystem syndrome associated with COVID-19 in Iran. BMC Pediatr 2020; 20(1): 513.
80. Hoseininasab A, Sinaei R, Bagheri MM, Ahmadipour M, Derakhshan R, Najafzadeh MJ, et al. Multisystem inflammatory syndrome in children (MIS-C) post-COVID-19 in Iran: clinical profile, cardiac features, and outcomes. BMC Pediatrics 2024; 24(1): 179.
81. Vafaee Shahi M, Vahedi Z, Behmadi R, Yousefzadegan S, Mousavi A, Mahdvnia S, Mahmoudabadi R. Clinical Characteristics, Treatment, and Outcomes of Multisystem Inflammatory Syndrome in Children Associated with COVID-19: A Single-Center Study from Iran. Journal of Comprehensive Pediatrics 2025; 16: e161545.
82. Levin M. Childhood Multisystem Inflammatory Syndrome - A New Challenge in the Pandemic. N Engl J Med 2020; 383(4): 393-5.
83. Hennon TR, Penque MD, Abdul-Aziz R, Alibrahim OS, McGreevy MB, Prout AJ, et al. COVID-19 associated Multisystem Inflammatory Syndrome in Children (MIS-C) guidelines; a Western New York approach. Prog Pediatr Cardiol 2020; 57(17): 101232.
84. Riollano-Cruz M, Akkoyun E, Briceno-Brito E, Kowalsky S, Reed J, Posada R, et al. Multisystem inflammatory syndrome in children related to COVID-19: A New York City experience. J Med Virol 2021; 93(1): 424-33.

85. García-Salido A, de Carlos Vicente JC, Belda Hofheinz S, Balcells Ramírez J, Slöcker Barrio M, Leóz Gordillo I, et al. Severe manifestations of SARS-CoV-2 in children and adolescents: from COVID-19 pneumonia to multisystem inflammatory syndrome: a multicentre study in pediatric intensive care units in Spain. Crit Care 2020; 24(1): 666.
86. Harwood R, Allin B, Jones CE, Whittaker E, Ramnarayan P, Ramanan AV, et al. A national consensus management pathway for paediatric inflammatory multisystem syndrome temporally associated with COVID-19 (PIMS-TS): results of a national Delphi process. Lancet Child Adolesc Health 2021; 5(2): 133-41.
87. Dove ML, Jaggi P, Kelleman M, Abuali M, Ang JY, Ballan W, et al. Multisystem Inflammatory Syndrome in Children: Survey of Protocols for Early Hospital Evaluation and Management. J Pediatr 2021; 229: 33-40.
88. Whitworth H, Sartain SE, Kumar R, Armstrong K, Ballester L, Betensky M, et al. Rate of thrombosis in children and adolescents hospitalized with COVID-19 or MIS-C. Blood 2021; 138(2): 190-8.
89. Gaitonde M, Ziebell D, Kelleman MS, Cox DE, Lipinski J, Border WL, Sachdeva R. COVID-19-Related Multisystem Inflammatory Syndrome in Children Affects Left Ventricular Function and Global Strain Compared with Kawasaki Disease. J Am Soc Echocardiogr 2020; 33(10): 1285-7.
90. Levy M, Recher M, Hubert H, Javouhey E, Fléchelles O, Leteurtre S, Angoulvant F. Multisystem Inflammatory Syndrome in Children by COVID-19 Vaccination Status of Adolescents in France. JAMA 2022; 327(3): 281-3.
91. Zambrano LD, Newhams MM, Olson SM, Halasa NB, Price AM, Boom JA, et al. Effectiveness of BNT162b2 (Pfizer-BioNTech) mRNA Vaccination Against Multisystem Inflammatory Syndrome in Children Among Persons Aged 12-18 Years - United States, July-December 2021. MMWR Morb Mortal Wkly Rep 2022; 71(2): 52-8.
92. Yousaf AR, Cortese MM, Taylor AW, Broder KR, Oster ME, Wong JM, et al. Reported cases of multisystem inflammatory syndrome in children aged 12-20 years in the USA who received a COVID-19 vaccine, December, 2020, through August, 2021: a surveillance investigation. Lancet Child Adolesc Health 2022; 6(5): 303-12.
93. Nygaard U, Holm M, Bohnstedt C, Chai Q, Schmidt LS, Hartling UB, et al. Population-based Incidence of Myopericarditis After COVID-19 Vaccination in Danish Adolescents. Pediatr Infect Dis J 2022; 41(1): e25-e8.